REMARKS

Claims 1-41 were pending in the instant application. Claims 3, 6, 12, 13 and 19-41 have been canceled without prejudice or disclaimer, claims 1, 2, 4, 5, 8, 10, and 11 have been amended, and new claims 42-48 have been added. In addition, pages 1, 7 and 9 of the specification have been amended. Accordingly, claims 1, 2, 4, 5, 7-11, 14-18, and 42-48 will be pending in the application upon entry of the instant claim amendments and additions.

Claims 13 and 19-41 have been cancelled as being drawn to non-elected subject matter (*i.e.*, Groups II through VII as set forth in an Office Action (Paper No. 9) dated June 23, 1999 and new Group IX including claim 13, as set forth in paragraph 1 of the Office Action (Paper No. 11) mailed October 14, 1999). Applicants hereby reserve the right to pursue non-elected subject matter of the cancelled claims in one or more divisional applications.

The specification has been amended to make specific reference to the earlier filed provisional application to which Applicants claim priority under 35 U.S.C. §119(e). In particular, the specification has been amended to recite the serial number of the earlier-filed provisional application, as requested by the Examiner in paragraph 2 of the instant Office Action. The specification has also been amended at pages 7 and 9 to incorporate text from the specification of provisional application no. 60/073,674. The content of the provisional application was incorporated by reference into the instant application as indicated on page 1, lines 3-4, of the instant application. Pursuant to M.P.E.P. §608.01(p), Applicants declare that the text added by amendment herein to pages 7 and 9 of the instant specification is the same as the material appearing a pages 11 and 3, respectively, of provisional application serial no. 60/073,674 filed February 4, 1998.

Support for the amendment to claims 1, 2, 4 and 5 can be found in the instant specification at least, for example, at page 3, lines 31-33. Support for the amendment to claim 8 can be found in the instant specification at least, for example, at page 9, in the text incorporated from provisional application no. 60/073,674. Support for the amendment to claims 11 and 12 can be found in the instant specification at least, for example, at page 7, in the text incorporated from provisional application no. 60/073,674. Support for new claims 42-45 can be found in the specification at least, for example, at page 9, lines 3-8, as well as in Example 9. Support for new claim 46 can be found in the specification at least, for example, at page 3, lines 33-36. No new matter has been added. Applicants request that the specification and claim amendments and the new claims be entered. For the Examiner's convenience, a copy of the claims which will be pending after the entry of this Amendment is provided as Appendix A.

Cancellation and amendment of claims should in no way be construed as an acquiescence to any of the rejections in the instant Office Action or any previous Office Action and were done solely to claim more fully Applicants' invention, and to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or one or more separate applications.

Priority

On page 2, paragraph 4, the instant Office Action indicates that "the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claim 1 of this application. There it is alleged that the "[c]laim 1 limitation directed to 'at least about 70% homologous to a nucleotide sequence of SEQ ID NO:1 or a complement thereof' is not disclosed in the provisional application no. 60/073,674. Without acquiescing to the objection and in order to expedite prosecution, Applicants have amended claim 1 to recite the phrase "at least 80% identical the

nucleotide sequence of SEQ ID NO:1", a recitation which Applicants respectfully submit is fully supported by the provisional application no. 60/073, 674 at page 4, lines 17-20.

The Office Action also indicates that the "[c]laims 1, 2, and 5 limitation directed to 'a complement thereof' is not disclosed in the provisional application no. 60/073,674". Without acquiescing to the objection and in order to expedite prosecution, Applicants have amended claims 1, 2 and 5. As amended, claims 1, 2 and 5 no longer recite the phrase "a complement thereof". Moreover, Applicants respectfully submit that the presently pending claims reciting the phrase "a complement of the nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1", for example, claims directed to isolated nucleic acid molecules which hybridize to "a complement of the nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1", are fully supported by the provisional application no. 60/073, 674. In particular, provisional application no. 60/073,674 describes and/or exemplifies such nucleic acid molecules at least, for example, at page 10, line 33 through page 12, line 5; as well as in Examples 1, 2, 4 and 9.

The Office Action further indicates that the "[c]laim 3 limitation directed to '1922-2341 of SEQ ID NO:1' is not disclosed in the provisional application no. 60/073,674", that the "[c]laim 4 limitation directed to '3136-3622 of SEQ ID NO:1' is not disclosed in the provisional application no. 60/073,674" and that the "[c]laim 6 limitation directed to '1922-2341 and 3136-3622 of SEQ ID NO:1' are not disclosed in the provisional application no. 60/073,674. Without acquiescing to the objection and in order to expedite prosecution, Applicants have cancelled claims 3 and 6 and have amended claim 4. As amended, claim 4 no longer recites the phrase "3136-3622 of SEQ ID NO:1". Moreover, none of the presently pending claims recites the phrases "1922-2341 of SEQ ID NO:1" and/or "3136-3622 of SEQ ID NO:1".

The Office Action also alleges that the "[c]laim 8 limitation directed to 'at least about 70% homologous to the amino acid sequence of SEQ ID NO:2' is not disclosed in

the provisional application no. 60/073,674. Without acquiescing to the objection and in order to expedite prosecution, Applicants have amended claim 8 such that it no longer recites the phrase "at least about 70% homologous to the amino acid sequence of SEQ ID NO:2". Moreover, Applicants submit that recitation of the phrase "which is substantially identical to the amino acid sequence of SEQ ID NO:2" in claim 8, as amended, is fully supported by provisional application no. 60/073,674, for example, at page 3, lines 20-34.

The instant Office Action further indicates that the "[c]laims 10-11 limitation directed to 'hybridizes under stringent hybridization conditions' is not disclosed in the provisional application no. 60/073,674". Applicants respectfully submit that nucleic acid molecules which "hybridize under stringent conditions" are fully described in provisional application no. 60/073,674, at least for example, at page 11, lines 20-29. However, in order to claim more fully the subject matter of claims 10 and 11, the enumerated claims have been amended to recite specific stringent hybridization conditions taught in provisional application no. 60/073,674 at page 11, lines20-29 (*e.g.*, hybridization conditions of hybridization in 50% formamide at 42°C followed by washing in 1XSSC/0.1%SDS at 65°C"). Moreover, the specification of the instant application has been amended to incorporate such exemplary hybridization conditions from provisional application no. 60/073,674, *e.g.*, at page 7, line 14 of the instant specification.

In addition, the Office Action indicates that the "[c]laim 11 limitation directed to 'at least 500 nucleotides in length which hybridizes under stringent hybridization conditions' is not disclosed in the provisional application no. 60/073,674". Without acquiescing to the objection and in order to expedite prosecution, Applicants have amended claim 11 such that it no longer recites the phrase "at least 500 nucleotides in length which hybridizes under stringent hybridization conditions". Claim 11, as amended, is directed to isolated nucleic acid molecules "at least 1000 nucleotides in length" which hybridize "under hybridization conditions of 50% formamide at 42°C

followed by washing in 1XSSC/0.1%SDS at 65°C". Applicants submit that such nucleic acid molecules are described in provisional application no. 60/073,674, at least for example, at page 4, lines 20-22 and at page 11, lines 10-29. Moreover, it is Applicants' position that new claims directed to isolated nucleic acid molecules at least 100 (or 200) nucleotides in length which hybridize under hybridization conditions of 50% formamide at 42°C followed by washing in 1XSSC/0.1%SDS at 65°C are likewise supported by the instant specification at page 12, lines 19-23, and at page 14, lines 4-12.

Lastly, the Office Action alleges that the "[c]laim 12 limitation directed to 'which specifically detects a RAC3 nucleic acid molecule relative to a nucleic acid molecule encoding a non-RAC3 protein' is not disclosed in the provisional application no. 60/073,674. Without acquiescing to the objection and in order to expedite prosecution, claim 12 has been cancelled. Moreover, none of the presently pending claims recites the phrase "which specifically detects a RAC3 nucleic acid molecule relative to a nucleic acid molecule encoding a non-RAC3 protein".

In view of the above-described claim amendments, claim cancellations and arguments, Applicants respectfully submit that the presently pending claims are fully supported by provisional application no. 60/073,674, upon which the priority claim of the instant application is based.

Specification Objections

In paragraph 4 on page 4, the instant Office Action sets forth an objection to the specification for allegedly "failing to provide proper antecedent basis for the claimed subject matter". In particular, the Office Action alleges that "[c]laims 3-4 and 6 are directed to the limitations '1922-2341 of SEQ ID NO:1', '3136-3622 of SEQ ID NO:1', or '1922-2341 and 3136-3622 of SEQ ID NO:1', respectively, which are not disclosed in the specification". As set forth above and reiterated here, claims 3 and 6 have been

cancelled and claim 4 has been amended such that it no longer recites the phrase "3136-3622 of SEQ ID NO:1". Accordingly, Applicants respectfully request that the Examiner reconsider the objection to the specification.

Information Disclosure Statement

In paragraph 5 on page 4, the Office Action indicates that "[t]he information disclosure statement filed 10 February 1999 (Paper No. 6) fails in part to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the list of references labeled AE-BP do not have a date in the form 1449". Applicants intend to submit, *via* hand delivery, a supplemental Information Disclosure and Form PTO-1449 setting forth "publication" dates for each of references AE-BP. Applicants invite the Examiner's attention to the fact that the "publication" date appearing on each of references AE-BP, which are printouts of electronic database records, corresponds to a date on which the cited electronic record was ***either*** first made publicly available ***or*** revised. In the case of revised records, Applicants further invite the Examiner's attention to the fact that earlier versions of such electronic records may have been available prior to the "publication" date appearing in the Form PTO-1449 submitted with the Supplemental Information Disclosure Statement. However, Applicants are unaware of the content of such earlier versions, and of the nature of the data added or revised with each revision of such electronic records.

Claim Rejections – 35 U.S.C. §112

Rejection of Claims 3, 4, and 6 Under 35 U.S.C. §112, First Paragraph

Claims 3, 4, and 6 are rejected under 35 U.S.C. §112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention". In particular, claims 3, 4, and 6 are rejected because of the recitation "further comprises". The Office Action alleges that "the specification does not disclose isolated nucleic acid molecule which 'further comprises' additional sequence of SEQ ID NO:1 sequences". Applicants respectfully traverse the rejection.

Claims 3 and 6 have been cancelled thus obviating the rejection at least as it may have been deemed pertinent to claims 3 and 6. Claim 4 has been amended. As amended, claim 4 no longer recites the phrase "further comprises". Accordingly, Applicants request reconsideration and withdrawal of the rejection of claim 4 under 35 U.S.C. 112, first paragraph.

Rejection of Claims 1-8, 10-12 and 14-18 Under 35 U.S.C. §112, Second Paragraph

Claims 1-8, 10-12 and 14-18 are rejected under 35 U.S.C. §112, first paragraph, as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention".

In particular, claims 3, 4 and 6 are rejected because of the recitation "further comprising". As stated previously and reiterated here, claims 3 and 6 have been cancelled and claim 4, as amended, no longer recites the phrase "further comprising".

In addition, claims 1, 2 and 5 are rejected because of the recitation "complement thereof". In particular, the Office Action indicates that "[i]t is not clear whether the term is referring to the fully complementary sequence or any fragment which is a complementary sequence. Applicants respectfully traverse the rejection.

Applicants submit that an ordinarily skilled artisan would have known what was meant by the language "complement thereof", given the teachings of the instant specification. However, without acquiescing to the rejection and in order to expedite

prosecution, claim 3 has been cancelled and claims 1, 2 and 5 have been amended so that they no longer recite "complement thereof". Accordingly, Applicants respectfully request that the rejection of claims 1, 2 and 5 under 35 U.S.C. §112, second paragraph, be withdrawn.

Claims 10 and 12 are rejected because of the recitation of the phrase "stringent hybridization conditions" which, as indicated in the Office Action, "is a relative term rendering the claims indefinite because the metes and bounds of the limitations are not clear". Applicants respectively traverse the rejection.

Applicants submit that an ordinarily skilled artisan would have known what was meant by the language "stringent hybridization conditions", given the teachings of the instant specification. However, without acquiescing to the rejection and in order to expedite prosecution, claim 12 has been cancelled and claim 10 has been amended so that it no longer recites "stringent hybridization conditions". Accordingly, Applicants respectfully request that the rejection of claims 10 and 12 under 35 U.S.C. §112, second paragraph, be withdrawn.

Claims 1, 3, 4, 6-8, 12, 14-18 are rejected because of the recitation of percent homology or identity. In particular, the Office Action alleges that "[t]he state of the art is such that one skilled in the art cannot determine what the meaning of the term 'identity' is without a precise algorithm with parameters i.e. 'scoring rules'". Applicants respectfully disagree.

With respect to claims 4, 7 and 14-18, Applicants submit that determination of percent identity is not *per se* indefinite. Applicants respectfully assert that, in view of the teachings of the specification and accepted practices in the art, it would be clear to the ordinarily skilled artisan that when determining percent identity, sequences are to be aligned such that an optimal alignment is achieved. Once an optimal alignment is achieved, determination of the percent identity between the sequences is a matter of

routine practice to one of skill in the art. Thus, regardless of the existence of a number of different alignment algorithms, the specification demonstrates and one of ordinary skill in the art would use an optimal alignment for sequence comparison purposes and determination of percent identity. Applicants respectfully assert that claims 4-7 and 14-18 reciting percent identity clearly set forth the metes and bounds of the claims. With regard to claims 3, 6 and 12, these claims have been cancelled, thus obviating the rejection at least as it may have been deemed pertinent to the enumerated claims.

For the foregoing reasons, Applicants submit that the claims meet the requirements of 35 U.S.C. §112, second paragraph, and respectfully request that the rejection of the claims under 35 U.S.C. §112, second paragraph, be withdrawn.

Claim Rejections – 35 U.S.C. §102

Rejection of Claims 1-12 and 14-18 Under 35 U.S.C. 102(a)

Claims 1-12 and 14-18 are rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Anzick et al. ((AA); Science, 1997). The Office Action alleges that Anzick *et al.* disclose "an isolated nucleic acid molecule encoding AIB1 which is a coactivator of a nuclear receptor (page 965, middle column). In particular, the Office Action indicates that "[a]lthough AIB1 has a different name from the claimed RAC3, it is structurally identical to AIB1 protein except for the number of glutamines at the C-terminus (Figure 1)". The Office Action cites Figure 4 of Anzick *et al.* as disclosing "the cell comprising the vector comprising the DNA encoding AIB1 and the method of producing the protein using the cell (page 968, footnote 16)" and cites Figures 2 and 3 as disclosing "nucleic acid hybridization of FISH and Northern analysis, respectively, using hybridizing probes". The Office Action further indicates that "[t]he cDNA isolated in the vector is double stranded, thus meeting the limitation of 'complement thereof'".

Applicants respectfully traverse the rejection, and assert that they have a date of invention that is prior to the publication date of the Anzick *et al.* reference. In support of this assertion, Applicants submit herewith an unexecuted declaration pursuant to 37 CFR §1.131 which Applicants declare that they had completed the invention as described and claimed in the instant patent application in this country prior to ***August 5, 1997***. The Anzick *et al.* reference cited by in the Office Action was published on ***August 15, 1997***. Applicants will forward the executed declaration as soon as possible.

Applicants respectfully submit that the invention disclosed in the present patent application was reduced to practice by the inventors prior to the effective date of the Anzick *et al.* reference. As such, the Anzick *et al.* reference is not available as prior art against the present invention under 35 U.S.C. §102(a). Accordingly, Applicants respectfully request reconsideration and withdraw of the rejection of the claims under 35 U.S.C. 102(a) as anticipated by Anzick *et al.*.

Claim Rejections – 35 U.S.C. §103

Rejection of Claims 1-12 and 14-18 Under 35 U.S.C. 103(a)

Claims 1-12 and 14-18 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Anzick *et al.* ((AA); Science, 1997) in view of Li *et al.* ((AC); PNAS, 1997) and Hardy *et al.* ((U); J. Clin. Endocrinol. Metabol., 1996). The Office Action relies on Anzick *et al.* for the reasons set forth above. The Office Action further indicates that Li et *al.* discloses "an isolated nucleic acid molecule encoding RAC3 which is a coactivator of a nuclear receptor". In particular, the Office Action cites Figures 1-3 and 5 of the Li et al. reference as disclosing a "cell comprising the vector comprising the DNA encoding AIB1 (sic) and the method of producing the protein using the cell". With regards to the Li et al. reference, the Office Action indicates that "[a]lthough the nucleic acid molecule was isolated from the same laboratory as the claimed inventors, the

reference has additional authors". The Office Action further cites Hardy *et al.* as teaching "that CAG codon repeat which encodes glutamines in the androgen receptor disrupts function is correlated with age of onset of prostate cancer (page 4400). Hardy et al. teach that CAG codon repeats are polymorphic in humans". The Office Action sets forth the conclusion that:

> It would be obvious to one of ordinary skill in the art at the time of the invention to isolate or modify the DNA of Anzick et al. to comprise different numbers of glutamine repeats because the Li et al. and Hardy et al. teach that the glutamine polymorphism with varying numbers of glutamine repeats is common in humans. Furthermore motivation is provided by Li et al. who teach the importance of mutagenesis experiments in providing further insights into the mechanism of receptor-coactivator interaction (page 8483, second column, first paragraph) especially in light of interest in the glutamine rich domain by Li et al. (page 8481, second column, first paragraph) and Anzick et al. (page 965, third column, first paragraph).

Applicants respectfully traverse the rejection, and assert that the Li *et al.* reference is not prior art under 35 U.S.C. § 103(a). In support of this assertion, Applicants submit herewith declaration, executed by Applicants, pursuant to 37 CFR §1.132 which indicates that Paulo J. Gomes, who is a co-author with inventors J. Don Chen and Hui Li of the Li *et al.* reference, is *not* a co-inventor of the subject matter described and claimed in the instant patent application. As indicated in the declaration, Paulo J. Gomes provided only technical assistance to Drs. J. Don Chen and Hui Li in performing the work described in the Li *et al.* reference.

Accordingly, the Li *et al.* reference represents Applicants' own work, published within one year of the filing of the present application, and cannot be used against Applicants under 35 U.S.C.§ 103(a). *In re Katz*, 687 F.2d 450, 215 USPQ 14 (CCPA 1958).

Moreover, for reasons discussed above, the Anzick *et al.* reference is not available as prior art against the present invention. In the absence of the teachings of the Anzick *et al.* and Li *et al.* references, Applicants assert that the claimed invention is not obvious in view of the teachings of the only remaining reference, namely the Hardy et al. reference.

Applicants respectfully submit that in view of the accompanying declarations pursuant 37 CFR §§1.131 and 1.132, the aforementioned rejection is rendered moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

SUMMARY

Applicants submit that all pending claims are presently in condition for allowance. If a telephone conversation with Applicants' attorney would expedite allowance of the above-identified application, the Examiner is urged to call Applicants' attorney at (617) 227-7400.

Date: April 14, 2000

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Enclosures (unexecuted Rule 131 Declaration; executed Rule 132 Declaration)

APPENDIX A

1. (Amended) An isolated nucleic acid molecule which encodes a RAC3 protein, comprising a nucleotide sequence at least 80% identical to the nucleotide sequence of SEQ ID NO:1.

2. (Amended) The isolated nucleic acid molecule of claim 1 comprising the coding sequence of SEQ ID NO:1.

4. (Amended) The isolated nucleic acid molecule of claim 1 comprising a nucleotide sequence at least 90% identical to the nucleotide sequence of SEQ ID NO:1.

5. (Amended) The isolated nucleic acid molecule of claim 1 comprising the nucleotide sequence of SEQ ID NO:1.

7. The isolated nucleic acid molecule of claim 1, having a RAC3 activity.

8. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence encoding a protein which comprises an amino acid sequence which is substantially identical to the amino acid sequence of SEQ ID NO:2.

9. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a protein which comprises the amino acid sequence of SEQ ID NO:2.

10. (Amended) An isolated nucleic acid molecule encoding a RAC3 protein comprising a nucleotide sequence which hybridizes under hybridization conditions of hybridization in 50% formamide at 42°C followed by washing in 1XSSC/0.1%SDS at 65°C to a nucleic acid molecule which is the complementary sequence of SEQ ID NO:1.

11. (Amended) An isolated nucleic acid molecule at least 1000 nucleotides in length which encodes a RAC3 protein, wherein said nucleic acid molecule hybridizes under hybridization conditions of hybridization in 50% formamide at 42°C followed by washing in 1XSSC/0.1%SDS at 65°C to a nucleic acid molecule which is the complementary sequence of SEQ ID NO:1.

14. A vector comprising the nucleic acid molecule of claim 1.

15. The vector of claim 14, which is a recombinant expression vector.

16. A host cell containing the vector of claim 15.

17. A method for producing RAC3 protein comprising culturing the host cell of claim 16 in a suitable medium until RAC3 protein is produced.

18. The method of claim 17, further comprising isolating RAC3 protein from the medium or the host cell.

42. (New) An isolated nucleic acid molecule at least 200 nucleotides in length which encodes a RAC3 protein comprising an N-terminal steroid receptor interacting domain which is substantially identical to amino acids 613 to 752 of SEQ ID NO:2, wherein said nucleic acid molecule hybridizes under hybridization conditions of hybridization in 50% formamide at 42°C followed by washing in 1XSSC/0.1%SDS at 65°C to a nucleic acid molecule which is the complementary sequence of SEQ ID NO:1.

43. (New) The isolated nucleic acid molecule of claim 42 which encodes a RAC3 protein comprising amino acids 613 to 752 of SEQ ID NO:2.

44. (New) An isolated nucleic acid molecule at least 200 nucleotides in length which encodes a RAC3 protein comprising a C-terminal transactivating domain which is substantially identical to amino acids 1018 to 1179 of SEQ ID NO:2, wherein said nucleic acid molecule hybridizes under hybridization conditions of hybridization in 50% formamide at 42°C followed by washing in 1XSSC/0.1%SDS at 65°C to a nucleic acid molecule which is the complementary sequence of SEQ ID NO:1.

45. (New) The isolated nucleic acid molecule of claim 42 which encodes a RAC3 protein comprising amino acids 1018 to 1179 of SEQ ID NO:2.

46. (New) An isolated nucleic acid molecule which encodes a RAC3 protein, comprising a nucleotide sequence at least 90% identical to the nucleotide sequence of SEQ ID NO:1.